

CLAIMS

1. An isolated nucleic acid molecule which comprises a sequence encoding a protein which inhibits osteoclast differentiation from haematopoietic cell precursors,  
5 selected from the group consisting of osteoclast inhibitory lectin (OCIL) and OCIL-related protein, and which is either  
(i) able to hybridize under conditions of moderate to high stringency to one or more sequences selected from the group consisting of SEQ ID NO: 2, SEQ ID  
10 NO: 4, SEQ ID NO: 7, SEQ ID NO: 8, SEQ ID NO: 9, SEQ ID NO: 10, SEQ ID NO: 11, SEQ ID NO: 12, SEQ ID NO: 15, SEQ ID NO: 19, SEQ ID NO: 20, SEQ ID NO: 21, SEQ ID NO: 33, SEQ ID NO: 36, SEQ ID NO: 37, SEQ ID NO: 44, SEQ ID NO: 45 and SEQ ID NO: 46 or selected from the group consisting of SEQ ID  
15 NO: 11, SEQ ID NO: 21, and SEQ ID NO: 37; or  
(ii) has greater than 80% sequence identity with one or more of the sequences set out in (i).
2. A nucleic acid molecule according to claim 1, which encodes a type II membrane protein.
- 20 3. A nucleic acid molecule according to claim 1 or claim 2, which is expressed at least by osteoblasts.
4. A nucleic acid molecule according to any one of claims 1 to 3, which is of human, mouse or rat origin.
5. A nucleic acid molecule according to any one of  
25 claims 1 to 3, which is a cDNA.
6. A nucleic acid molecule according to claim 5, in which the cDNA comprises a sequence selected from the group consisting of SEQ ID NO: 2, SEQ ID NO: 4, SEQ ID NO: 7, SEQ ID NO: 8, SEQ ID NO: 9, SEQ ID NO: 10, SEQ ID NO: 12, SEQ  
30 ID NO: 15, SEQ ID NO: 19, SEQ ID NO: 20, SEQ ID NO: 33, SEQ ID NO: 36, SEQ ID NO: 44, SEQ ID NO: 45 and SEQ ID NO: 46.
7. A nucleic acid molecule according to any one of claims 1 to 4, which is a gDNA.
8. A nucleic acid molecule according to any one of  
35 claims 1 to 4, in which the gDNA comprises a sequence selected from the group consisting of SEQ ID NO: 11, SEQ ID

- 59 -

NO: 21, and SEQ ID NO: 37, or which hybridises to said nucleic acid molecule under stringent conditions.

9. A nucleic acid molecule according to any one of claims 1 to 8, which encodes an extracellular domain of an OCIL or of an OCIL-related protein.

10. A nucleic acid molecule according to any one of claims 1 to 9, which encodes a protein which inhibits differentiation of haematopoietic stem cells to osteoclast progenitor cells.

11. A nucleic acid molecule according to any one of claims 1 to 10, which comprises a 110 base pair sequence as set out in SEQ ID NO: 2.

12. An anti-sense sequence directed against a nucleic acid molecule according to any one of claims 1 to 11.

13. An anti-sense sequence according to claim 12, directed against SEQ ID NO: 10.

14. An anti-sense sequence according to claim 12 or claim 12, which is SEQ ID NO: 24 or SEQ ID NO: 25.

15. An isolated polypeptide encoded by a nucleic acid molecule according to any one of claims 1 to 11.

16. A polypeptide according to claim 15, which is encoded by the human cDNA or gDNA sequence.

17. A polypeptide according to claim 16, which is encoded by the mouse cDNA or gDNA sequence.

18. A polypeptide according to claim 17, comprising a sequence selected from the group consisting of SEQ ID NO: 40, SEQ ID NO: 41, and SEQ ID NO: 42.

19. A polypeptide according to claim 15, which comprises an amino acid sequence encoded by SEQ ID NO: 20.

20. An isolated polypeptide selected from the group consisting of a C-lectin motif, an extracellular domain, a transmembrane domain, or a cytoplasmic domain of a polypeptide according to any one of claims 15 to 19.

21. An antibody directed against a polypeptide according to any one of claims 15 to 20.

- 60 -

22. An antibody according to claim 21, which is directed against an epitope present in a sequence selected from the group consisting of  
Cys-Met-Ala-Gln-Glu-Ala-Gln-Leu-Ala-Arg-Phe-Asp-Asn-Gln-  
5 Asp-Glu-Leu-Asn-Phe (SEQ ID NO: 26).  
Cys-Val-Thr-Lys-Ala-Ser-Leu-Pro-Met-Leu-Ser-Pro-Thr- Gly-  
Ser-Pro-Gln-Glu (SEQ ID NO: 48), and  
Cys-Val-Gln-Lys-Pro-Glu-Glu-Gly-asn-Gly-Pro-Leu-Gly-Thr-  
Gly-Asp (SEQ ID NO: 49).
- 10 23. An antibody according to claim 21 or claim 22, which is monoclonal.
24. A composition comprising a polypeptide according to any one of claims 15 to 20, together with a pharmaceutically-acceptable carrier.
- 15 25. A composition comprising an antibody according to any one of claims 21 to 23, together with a pharmaceutically-acceptable carrier.
26. A method of treatment of a condition characterised by abnormal bone resorption, comprising the  
20 step of administering an effective amount of a modulator of expression or function of a polypeptide according to any one of claims 15 to 20.
27. A method according to claim 26, in which the condition involves excessive bone resorption, and the  
25 method comprises administration of a polypeptide according to any one of claims 15 to 19, or a nucleic acid encoding this polypeptide, or encoding a biologically-active fragment or analogue thereof.
28. A method according to claim 27, in which the  
30 condition is selected from the group consisting of osteoporosis, primary hyperparathyroidism, Paget's disease, rheumatoid arthritis, renal osteodystrophy, humoral hypercalcaemia of malignancy, and conditions where cancer has metastasised to bone.
- 35 29. A method according to claim 26, in which the condition involves deficient bone resorption, and the method comprises administration of an antibody according to

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- 61 -

any one of claims 21 to 23 or an anti-sense oligonucleotide according to any one of claims 11 to 13.

30. A method according to claim 28, in which the condition is osteopetrosis.

5 31. A method of promoting healing of bone fractures, particularly in an individual in whom fracture healing is delayed or deficient, comprising the step of administering an effective amount of a polypeptide according to any one of claims 15 to 20.

10 32. A method according to claim 31, in which the individual is suffering from osteoporosis or diabetes mellitus.

33. A method of modulating breast and/or lymph node development, comprising the step of administering an  
15 effective amount of a modulator of expression or function of a polypeptide according to any one of claims 15 to 20 to a subject in need of such treatment.

34. A diagnostic kit for detection of abnormalities in the structure, expression or control of a type II  
20 membrane polypeptide expressed on the osteoblast cell surface, selected from the group consisting of osteoclast inhibitory lectin (OCIL) and OCIL-related protein, comprising a reagent selected from the group consisting of  
(a) a nucleic acid according to any one of claims 1  
25 to 11, or a fragment thereof capable of hybridising to a nucleic acid according to any one of claims 1 to 11;  
(b) an anti-sense nucleic acid according to any one of claims 12 to 14;  
30 (c) a polypeptide according to any one of claims 15 to 20, and  
(d) an antibody according to any one of claims 21 to 23.

35. A diagnostic kit according to claim 34, in which the reagent is labelled with a detectable marker.

36. A method of screening of candidate agents for treatment of a condition characterised by abnormal bone

- 62 -

resorption, comprising the step of assessing the ability of each agent to modulate expression or function of a polypeptide according to any one of claims 15 to 19.

37. An oligonucleotide primer selected from the  
5 group consisting of sense primers having the sequence set out in SEQ.ID. NO:5, 6, 30, 35, 13, 14, 16, 18, 27, 47, 50, 52, 54, or 55, and antisense primers having the sequence set out in SEQ.ID. NO: 3, 31, 32, 14, 28, 34, 38, 39, 51, 53, 22, 23, 24, 25, 43 or 56.

10 38. A polypeptide according to claim 18, comprising the sequence set out in SEQ ID NO:40.

39. An isolated polypeptide according to any one of claims 15 to 20, whose expression is differentially regulated by PTH or PTHrP.

15